

(d) during said maintaining, measuring photon emission from the animal with the photo detector device to detect the level of expression of the light generating polypeptide in a living animal wherein said expression is mediated by at least one of the control elements.

A<sup>2</sup> 78. The method of claim 77, further comprising, (e) repeating steps (b) through (d) at selected intervals, wherein said repeating is effective to detect changes in the level of the light emission in the animal over time.

79. The method of claim 78, wherein an increase in the expression of the light generating polypeptide in the presence of the analyte indicates potential toxicity of the analyte.--

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#### REMARKS

##### Introductory Comments

Claims 1-64 are pending. Claims 38 and 39 have been amended. Claims 1-37 and 51-64 have been canceled by this amendment. New claims 65-79 have been entered by this amendment.

The Examiner has imposed a restriction requirement on the originally presented claims.

##### Overview of the Amendments

To the Specification:

The amendments to the specification are being made to correct inadvertent, typographical errors which appeared in

the application as originally filed. The inadvertent errors are essentially as follows: "=" corresponded to an apostrophe; "A" corresponded to an opening quotation mark; and "@" corresponded to a closing quotation mark. The corrections are self-evident upon examination of the specification. If the Examiner wishes, applicants can provide a substitute specification.

Accordingly, no new matter has been added by way of these amendments and the entry thereof is respectfully requested.

To the Claims:

Claims 1-37 and 51-64 have been canceled without prejudice or disclaimer. Claims 38 and 39 have been amended without prejudice or disclaimer. Cancellation or amendment of these claims is not intended to be an acquiescence in the Office's assessment of those claims. Further, applicants expressly reserve the right to bring the subject matter of the original claims again in a subsequent, related application.

Basis for the amendments to claims 38 and 39 ("first and second expression cassettes") can be found throughout the specification, for example, at the following location: originally presented claim 1.

Basis for new claims 65-72 ("expression cassettes") can be found throughout the specification, for example, at the following location: originally presented claims 2-5.

The amendments to claims 38 and 39 constitute incorporating the limitations of independent claim 1 into claims 38 and 39, which originally depended from claim 1.

New claims 65-72 correspond to claims 2-5, now depending from independent claims 38 and 39.

Basis for new claims 73 and 79 can be found throughout the specification, for example, at the following locations: originally presented claim 40; page 35, lines 11-17; page 26, lines 16-18; page 26, line 27, to page 27, line 4; page 72, lines 11-14; page 4, line 27-29; page 60, lines 8-18; page 38, line 5; and page 42, line 28.

Basis for new claim 74 can be found throughout the specification, for example, at the following location: originally presented claim 41.

Basis for new claim 75 can be found throughout the specification, for example, at the following locations: originally presented claim 38; page 31, lines 21-22; and page 44, lines 30-33.

Basis for new claim 76 can be found throughout the specification, for example, at the following locations: page 33, line 26, to page 34, line 7; page 38, line 5; and page 42, line 28.

Basis for new claim 77 can be found throughout the specification, for example, at the following location: originally presented claim 45.

Basis for new claim 78 can be found throughout the specification, for example, at the following location: originally presented claim 46.

Accordingly, no new matter has been added by way of this amendment and the entry thereof is respectfully requested.

### RESPONSE TO RESTRICTION REQUIREMENT

In the Office action dated 17 July 2000 the Examiner made the following restriction requirement. The Examiner divided the claims into the following groups:

Group I: claims 1-5 and 36-64, "drawn to a panel of expression cassettes comprising two or more expression cassettes comprising regulatory elements of different stress-inducible genes, method of making a transgenic animal using the expression cassettes and the method of using the transgenic animals."

Group II, claims 6-10, "drawn to a panel of expression cassettes comprising two or more expression cassettes comprising regulatory elements of different apoptosis-related genes."

Group III, claims 11-15, "drawn to a panel of expression cassettes comprising two or more expression cassettes comprising regulatory elements of different angiogenesis-related genes."

Group IV, claims 16-20, "drawn to a panel of expression cassettes comprising two or more expression cassettes comprising regulatory elements of different development-related genes."

Group V, claims 21-25, "drawn to a panel of expression cassettes comprising two or more expression cassettes comprising regulatory elements of different oncogenesis-related genes."

Group VI, claims 26-30, "drawn to a panel of expression cassettes comprising two or more expression cassettes comprising regulatory elements of different genes expressed in response to an infection of a host by an infectious

agent."

Group VII, claims 31-35, "drawn to a panel of expression cassettes comprising two or more expression cassettes comprising regulatory elements of different inflammation-related genes."

The applicants provisionally elect group I, with traverse.

Applicants traverse the grouping of the claims for the following reasons. First, claims 51-64 are related to a method of producing a transgenic, non-human animal, said animal having at least one single-copy, non-essential gene in its genome. These claims represent a new method of generating transgenic animals and cohorts of transgenic animals. Thus, these claims would require a completely different search essentially unrelated to the "first and second expression cassettes" of claim 1 and as such should be grouped as a separate invention. A related claim set directed to the invention of claims 51-64 is being prosecuted in a different application. Accordingly, these claims have been canceled by this amendment.

In addition, applicants submit that Group I should be restricted into two further groups related to claims 38 and 39. Claim 38 is directed to a **single** transgenic, non-human animal comprising a panel of expression cassettes. Claim 39 is directed to a **cohort** of transgenic, non-human animals comprising a panel of expression cassettes, where (i) each transgenic animal of the cohort contains at least one expression cassette of the panel, and (ii) the transgenic animals comprising the cohort are substantially isogenic relative to each other. The specification defines "cohort"

as "a group of individuals having a statistical factor in common. In one aspect of the present invention, the statistical factor in common is that the individuals are substantially isogenic" (see, for example, page 21, lines 16-18). Applicants submit that a cohort of animals having the claimed limitations (i) and (ii) would require a very different search relative to a single transgenic animal. The differences between claims 38 and 39 are more apparent in view of applicants' amendments to these claims wherein the limitations of independent claim 1 have been incorporated into each of claims 38 and 39, and dependent claims, corresponding to original claims 2-5, have been added for each of claims 38 and 39.

In view of the amendments to claims 38 and 39, applicants submit the following new groups derived from Group I:

Group VIII, claims 38, 40, 41, 43, 45, 46, and 49, drawn to a transgenic, non-human animal comprising a panel of expression cassettes comprising two or more expression cassettes comprising regulatory elements of different stress-inducible genes, and methods of using the transgenic animals.

Group IX, claims 39, 42, 44, 47, 48, and 50, drawn to a cohort of transgenic, non-human animals comprising a panel of expression cassettes, where (i) each transgenic animal of the cohort contains at least one expression cassette of the panel, and (ii) the transgenic animals comprising the cohort are substantially isogenic relative to each other, and methods of use thereof.

Further, newly added claims 73-79 are distinct from the previously submitted claims, at least in that, claims 73-79

are directed to a single animal comprising one expression cassette and methods of use thereof. Accordingly, applicants submit that newly submitted claims 73-79 should be placed in a separate group, as follows:

Group X, claims 73-79, drawn to a transgenic, non-human animal comprising an expression cassette, said expression cassette comprising control elements derived from an H0 gene operably linked to sequences encoding a light generating protein, and methods of use thereof.

If the Examiner agrees with the applicants' new groupings, applicants elect Group VIII, claims 38, 40, 41, 43, 45, 46, and 49 (as amended) to begin prosecution.

If, however, the Examiner disagrees with the applicants' groupings, applicants request that the Examiner contact the undersigned before any further action is taken in prosecution. In this case applicants would like to discuss the groupings of the claims with the Examiner or, if the Examiner and applicants cannot reach an agreement, applicants will file a petition to request reconsideration of the groups.

Upon allowance of the generic claims, applicants request consideration of claims to additional species which are written in dependent form or which otherwise include all the limitations of the allowed generic claims.

Accordingly, applicants provisionally elect Group I, with traverse, to begin prosecution; however, applicants prefer to elect proposed Group VIII for the reasons presented above.

**CONCLUSION**

Applicants respectfully submit that the claims comply with the requirements of 35 U.S.C. §112 and define an invention that is patentable over the art. Accordingly, a Notice of Allowance is believed in order and is respectfully requested.

If the Examiner notes any further matters which the Examiner believes may be expedited by a telephone interview, the Examiner is requested to contact the undersigned.

Please direct all further communications in this application to:

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Respectfully submitted,

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